



Clip migration in stereotactic biopsy

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Abstract

Background: Needle localization breast biopsy (NLBB) is the standard for removal of breast lesions after vacuum assisted core biopsy (VACB). Disadvantages include a miss rate of 0% to 22%, a positive margin rate of approximately 50%, and vasovagal reactions (approximately 20%). We hypothesized that clip migration after VACB is clinically significant and may contribute to the positive margin rates seen after NLBB.

Methods: We performed a retrospective review of postbiopsy films in patients who had undergone VACB with stereotactic clip placement for abnormal mammograms. We measured the distance between the clip and the biopsy site in standard two view mammograms. The location of the biopsy air pocket was confirmed using the prebiopsy calcification site. The Pythagorean Theorem was used to calculate the distance the clip moved within the breast. Pathology reports on NLBB or intraoperative hematoma-directed ultrasound-guided breast biopsy (HUG, which localizes by US the VACB site) were reviewed to assess margin status.

Results: In all, 165 postbiopsy mammograms on patients who had VACB with clip placement were reviewed. In 93 evaluable cases, the mean distance the clip moved was $13.5 \text{ mm} \pm 1.6 \text{ mm}$, SEM (95% CI = 10.3 mm to 16.7 mm). Range of migration was 0 to 78.3 mm. The median was 9.5 mm. In 21.5% of patients the clip was more than 20 mm from the targeted site. Migration of the clip did not change with the age of the patient, the size of the breast or location within the breast. In the subgroup of patients with cancer, margin positivity (including those with close margins) after NLBB was 60% versus 0% in the HUG group.

Conclusions: Significant clip migration after VACB may contribute to the high positive margin status of standard NLBBs. Surgeons cannot rely on needle localization of the clip alone and must be cognizant of potential clip migration. HUG as an alternative biopsy technique after VACB eliminates operator dependency on clip location and may have superior results in margin status. © 2002 Excerpta Medica, Inc. All rights reserved.

Keywords: Core needle biopsy; Stereotaxis; Breast lesions; Clip placement

More than one million breast biopsies are performed per year in the United States [1], with an increasing number of these biopsies indicated for nonpalpable mammographic abnormalities. Prior to 1990, needle localization excisional breast biopsy (NLBB) was the only means of targeting

mammographic abnormalities. Percutaneous stereotactic core needle breast biopsy (SCNBB), first introduced by Parker [2] in 1990, is an accurate and less invasive alternative that is less costly than NLBB and provides a better rate of margin clearance when the diagnosis of cancer has been established prior to definitive procedure. This has influenced many surgeons in favor of SCNBB [3-7]. However, with increasing use of the vacuum-assisted core biopsy (VACB) device for SCNBB, all radiographic evidence of

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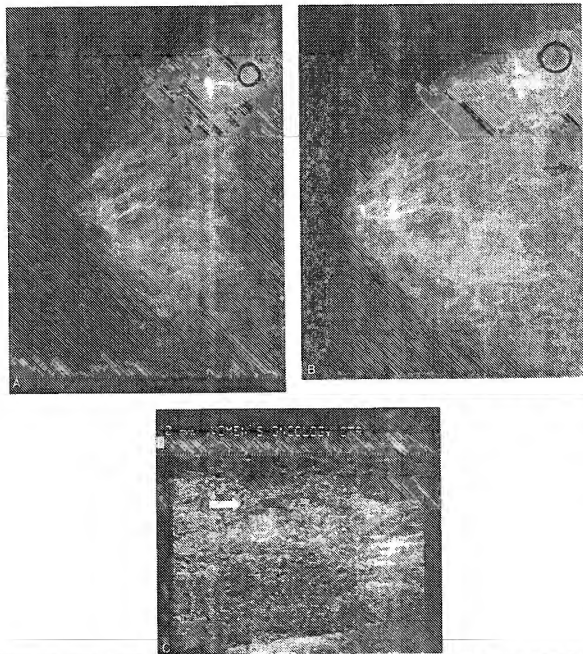


Fig. 1. (A) Encircled microcalcifications of a 49-year-old woman, as seen in the right cranial caudal view. (B) Clip (black arrow) migration from the biopsy site air pocket (black circle), after a vacuum-assisted core biopsy. Core pathology revealed ductal carcinoma in situ (DCIS), but subsequent localization on the clip failed to reveal evidence of the biopsy site. (C) Intraoperative ultrasound localization of biopsy site and needle tract hematoma (white arrow) guided excisional biopsy and allowed for pathological confirmation of biopsy site. No further evidence of DCIS was seen.

lesions are frequently removed [8,9], leading to the common practice of a stereotactic clip placement in the biopsy site at the time of SCNBB. When the results of SCNBB require further evaluation, NLBB that re-targets the biopsy site based on clip location has been the traditionally method for excisional biopsy. A potential caveat of this practice is that inaccuracies in technique or migration of the clip after placement may lead to localization errors requiring further

surgery for positive margins or missed lesions, as exemplified in Fig. 1.

We hypothesized that clip migration after SCNBB is clinically significant and may contribute to positive margin rates seen after NLBB. This retrospective review examining clip migration and offers intraoperative hematoma-directed ultrasound-guided breast biopsy (HUG) as an alternative localization technique that is clip independent.

Methods

Patients

Postbiopsy films of patients with abnormal mammograms who had undergone a VACB (a form of SCNBB), with clip placement were included in this study. From October 1998 through August 2001 all available films were retrospectively reviewed. The protocol for data collection was approved by the institutional review board. Inclusion criteria included ability to either visualize both clip and biopsy site on the standard two view mammograms post-procedure or ability to compare postprocedure films with preprocedure films in the same mediolateral or mediolateral oblique angle. An estimation of relative breast area was calculated for each evaluable case. This was performed by multiplication of craniocaudal and mediolateral diameters.

Stereotactic procedure

Stereotactic procedures were performed at the Arkansas Cancer Research Center by radiologists or members of the breast surgery team. VACB was performed on patients in the prone position on a dedicated stereotactic table (Mammotest; Fisher Imaging, Denver, Colorado) using an 11-gauge vacuum assisted Mammotome device (Biopsy Medical, Irving, California). After tissue removal, from October 1998 through July 15, 2001, in accordance with the mammotome instruction package, the stereotactic probe was pulled back 5 mm from biopsy position. A 2 mm clip (Micromark II; Ethicon Endo-Surgery, Cincinnati, OH) was then deployed through the probe into the biopsy site. Six month follow-up films were used to compare clip placement with biopsy site. Concern that the clip may not be attaching to the biopsy site led to a modification in clip deployment. Starting July 16, 2001, the biopsy probe was no longer pulled back 5 mm from the biopsy site prior to clip deployment. In addition, a standard two-view postprocedural mammogram was obtained after VACB.

Calculation of clip migration

Three-dimensional assessment of clip migration distance was calculated as shown in Fig. 2. In brief, the Pythagorean Theorem was applied to the series of two adjoining right triangles created using both the craniocaudal and mediolateral views. The adjoining side is the hypotenuse of both triangles and represents the true distance or migration of the clip from the biopsy site. The true distance was calculated twice, using two sets of adjoining right triangles, and then averaged. For cases of mediolateral oblique view, corrections for the degree off the perpendicular were geometrically adjusted for by using the cosine function. For these cases, the true distance was calculated based on the one available set of adjoining right triangles.

Surgical procedure

Lesions that revealed a pathological diagnosis of cancer, a risk of associated carcinoma (atypia), or that were discordantly benign with a suspicious mammogram were surgically excised either by mastectomy, NLBB or HUG as described by Smith et al [10] that localizes the core biopsy site based on the hematoma created by the stereotactic VACB procedure. Briefly, the hematoma is localized in the standard longitudinal planes and transverse planes. Dissection is then carried down toward the chest wall using a "line of site" technique [11]. Tissue is then excised around the hematoma in a block fashion to achieve a 1-cm margin. Excision of the targeted lesion was confirmed by direct visualization of the hematoma in the gross specimen as well as microscopically.

Pathology

Specimen margins were inked with six different colors for the six margins. Slides were stained with hematoxylin and eosin (H&E) and examined for evidence of malignancy. The specimen was serially sectioned at 5-mm intervals. Permanent margins were classified as positive if tumor cells were present at the inked margin, close if the lesion was less than 2 mm of the margin, and negative if the lesion was 2 mm or greater from the margin.

Statistics

The effects of age, clip location, breast size and stereotactic technique on clip migration distance were examined using correlation analysis, Cochran-Mantel Haenszel methods, and the Kruskal-Wallis Test.

Results

Patients

A total of 165 postbiopsy mammograms done on 160 patients (5 patients had bilateral procedures) who had VACB with clip placement were reviewed. The age of patients ranged from 34 to 93 years old with a mean age of 58 ± 0.9 SEM. Ninety-three films done on 91 patients met the inclusion criteria. Seventy-five of the evaluable VACB films were performed from October 1998 through July 15, 2001, the remainder (18), were performed after this date. In evaluable cases, the most frequent location (42 of 93) of lesions was the upper outer quadrant of the breast.

Stereotactic biopsy pathology

All 165 VACB specimens were sent to pathology for permanent H&E sections. Slides were reviewed at a weekly multidisciplinary breast conference with a single pathologist

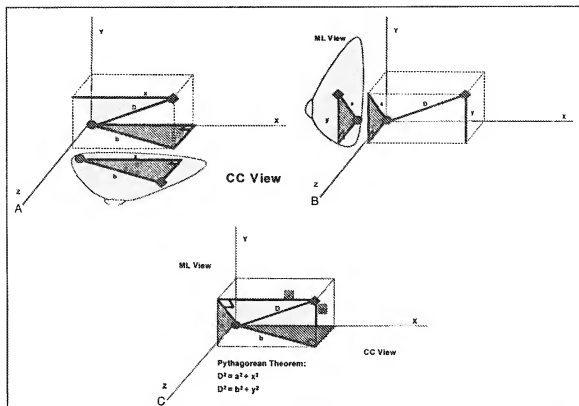


Fig. 2. (A) Relationship of biopsy site (circle) and clip location (diamond) and the distance between the two (line D), as depicted in three dimensions provided by the X, Y, and Z axis. In the forefront or XZ plane, is projection of the line D onto the cranial caudal (CC) view (line b). Note that line b is shorter than line D because it lacks depth. Line b is the hypotenuse of the right triangle that can be drawn in the CC view. Line "x" is the distance in the x axis that the clip moves on CC view and corresponds to same distance on the main rectangle in the figure. (B) Line D projects onto the mediolateral view as line "a." The right triangle drawn in the ML view provides the "y" distance that corresponds to the same distance in the main rectangle. (C) The shaded triangles from corresponding CC and ML views provide the distances for two more right triangles, "byD" and "axD," which share as their hypotenuse the line D. By the principle of the Pythagorean Theorem (the hypotenuse squared equals the sum of the squares of the triangle's legs), D, or the true distance in space that the clip travels, is calculated. The calculation can be performed using either formula listed and then averaged for improved accuracy.

(SK). VACB pathology indicated that 53 specimens from 52 patients (1 patient had bilateral specimens) would require surgical excision. Eight patients had infiltrating mammary carcinoma and 14 patients had ductal carcinoma in situ (DCIS). VACB showed the remaining patients requiring reexcision had lobular carcinoma in situ (LCIS)(1), atypical ductal hyperplasia (6), atypical lobular hyperplasia (4), papillomas (9), radial scar (2), fibroadenoma with atypia (1) and discordant pathology with mammographic findings (8). Ten of the 52 patients declined further surgical work-up. All ten patients had lesions that were associated with a higher risk for carcinoma but not frank cancer.

Clip migration

In the 93 evaluable cases, the mean distance that the clip moved was $13.5 \text{ mm} \pm 1.6 \text{ mm}$ (95% CI = 10.3 mm to 16.7 mm). The range of migration was 0 to 78.3 mm. The median was 9.5 mm with lower and upper quartiles of 3.0 mm and 16.4 mm, respectively. The mode was 0 mm. Fig. 3 depicts the frequency distribution. In 21.5% of patients the clip was more than 20 mm from the targeted site. There was no

significant difference in migration distances for procedures done prior to July 16, 2001 compared with those done at a later date. Migration of the clip did not change with size of the breast, location within the breast, or patient age.

Surgical procedure

Of 160 patients, 42 underwent surgical reexcision of VACB site for core pathology findings (43 specimens). There were a total of 9 mastectomies, 15 NLBBs, 18 HUGs based on VACB hematoma localization. One additional specimen was excised using a combination of NLBB and HUG. In the subgroup that had cancer (23 of 43 patients), there were 8 mastectomies performed, 8 NLBBs, 6 HUGs and 1 NLBB and HUG combination. One prophylactic mastectomy was performed in a patient with ADH and contralateral DCIS.

Excisional biopsy pathology

Excisional biopsy revealed that 23 (53%) of the excised lesions were malignant. Of the total of 165 specimens, 3

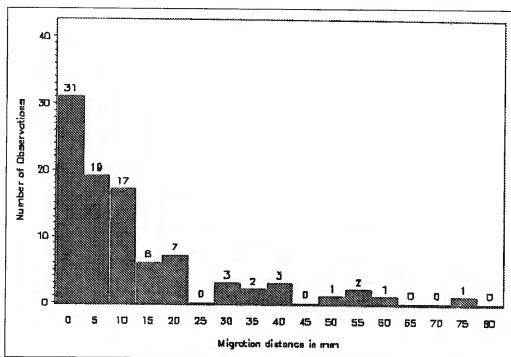


Fig. 3. Histogram of clip migration distance versus frequency.

NLBB were performed for cancer. Four specimens (50%) had negative margins, 2 (25%) had close margins, and 2 (25%) had positive margins. Six HUGs were performed for cancer. Five specimens (83%) had negative margins, none (0%) had close margins, and 1 (17%) had positive margins. One specimen performed using both NLBB and US had positive margins and was excluded from either group. In the subgroup of evaluable patients (91; 93 specimens) there were 5 NLBB that revealed malignancy. Two specimens that had negative margins had clip migration distances of only 3.5 mm and 0 mm, respectively. Two specimens with close margins had clip migration distances of 2 mm and 9 mm, respectively. One specimen with positive margins had a clip migration distance of 8.1 mm. Three specimens of the evaluable group performed by HUG revealed malignancy. All 3 specimens revealed negative margins; the clip distances for these specimens were 12.8 mm, 1 mm, and 1.6 mm, respectively.

Comments

With the current emphasis on increased screening mammography, a surgeon is frequently faced with the excision of nonpalpable breast lesions. SCNBB, first described by Parker [2] in 1990, has become the method of choice for the diagnostic biopsy of microcalcifications and other nonpalpable breast lesions. Cost savings may be as great as 50% when compared with NLBB [1,12,13]. SCNBB must be followed with a definitive procedure for cancer, atypia, other high risk lesions or when mammography and pathol-

ogy are discordant [14]. Frequently, all radiographic evidence of a lesion is removed after VACB, a figure reported between 50% and 72% [8,9]. In this situation, determining the most precise method of identifying the VACB biopsy site for subsequent excision or for long term follow-up (if the core pathology proves to be benign), remains controversial. NLBB has been the traditional method for excisional biopsy after SCNBB but relies on accurate SCNBB clip placement for localization. Other alternative methods have recently been reported and will be discussed below.

This study demonstrates that significant clip migration may occur after a VACB procedure. An inaccurately located clip may contribute to positive margin status on a subsequent NLBB. HUG provides an alternative to NLBB for clips that are both correctly and incorrectly targeted.

In our study we found that clip location can be an unreliable marker for the prior VACB site. Average clip migration was calculated to be 13.4 mm with 50% of the clips placed greater than 9.5 mm and 21.5% of clips greater than 20 mm from the biopsy site. Potential for clip migration has been reported by others [9,15-18]. However, clip migration may have been underestimated due to calculation of the distance while the breast was still in compression [15,17], which would not account for the potential of clip migration once the breast is released. Measurements that involve averaging distances measured on two-view mammograms rather than deriving the actual distance as the square root of the sum of the squares also could theoretically underestimate the distance [9,18]. Our method did not factor in baseline variability that would account for slight alterations in breast positioning that occur when the breast is

placed in the "same view." This variability, determined to be 7.7 mm in one study [9], would only be applicable to our early group that employed 6-month follow-up films for measurement purposes and could have potentially led to some overestimation of distance moved in that group. Justification for using 6-month follow-up films to document clip migration (for procedures done prior to July 16, 2001) was based on a previous study that demonstrated no further clip migration after an equivalent 6-month follow-up interval [9].

There is no clear explanation for clip migration. Certainly technical problems or inexperience of the physician placing the clip can be a factor. All surgeons and radiologists performing the procedure at our institution have the recommended experience [19] with the use of the 11-gauge VACB device. Alternative explanations include accurate clip placement without attachment to surrounding tissue and either retraction with the needle or migration, versus recoil with attached tissue after release of compression. Several modifications on clip products have been devised. Micro-coils have also been used to localize the site of breast lesions removed at stereotactic biopsy [20] as well as a collagen plug and clip system (MammoMark; Artemis Medical, Hayward, California) that aims to fill the biopsy cavity with collagen to limit clip movement and allow better visualization with US.

While increased use of large gauge VACB has led to improvements in the estimation of disease extent [21], it has not eliminated the need for accurate surgical excision. NLBB has been associated with positive margin status in the range of 51% to 57% [3,22]. Most positive margins after needle localization excision have been due to radiographic underestimation of disease extent [23]. However, localization on a migrated clip, rather than the true biopsy site could lead to positive margins even when specimen radiograph and pathological findings confirm both clip and biopsy site in the specimen. Although the sample size was too small to confer any significance to the findings, it was noted that two clip migrations that approached the median of 9.5 were associated with a close or positive margin status. In addition, a significant number of patients suffer problems in association with NLBB, including a miss rate ranging from 0% to as high as 22% [19,24,25], the possibility of wire transection, migration or dislocation [19,24], scheduling difficulties, vasovagal reactions in up to 20%, and the discomfort of having a wire or needle in the breast while the patient is awaiting surgery.

Alternative localization methods include carbon marking [26], use of methylene blue dye [27], radioactive seed placement [22], and the free hand needle technique [16]. The HUG technique utilizes the line of site principle and has many potential advantages over NLBB. It improves patient comfort and eliminates the need for an additional procedure with concomitant risks of complications and additional cost. Scheduling is simpler because it eliminates a visit to radiology preoperatively. The hematoma has been demonstrated

to remain visible up to 56 days after biopsy, longer than the average visibility of the clip and collagen system currently available. Methylene blue dye [27] and more recently carbon marking [26] stain the biopsy site and require visual tracking and removal of the entire needle tract. Radioactive seed localization [22] requires a second procedure for location and gamma expertise but has been shown to have a lower rate of margin positivity compared with standard needle localization in a small randomized series. Radioactive seed placement is based on an accurate clip placement.

Conclusions

Achieving tumor-free margins at the first surgical excision may play a role in decreasing recurrence rate. VACB relies heavily on accurate localization of the biopsy site. In approximately 20% of cases, clip placement at the time of VACB demonstrated potentially clinically significant migration. Therefore an immediate two-view mammogram is recommended after clip placement and release of stereotactic compression to document location of clip placement in relation to the biopsy site. When performing needle localization procedures that target on the clip location physicians should first verify the accuracy of clip placement. Ultrasound-guided excision (HUG), based on VACB hematoma localization, does not require a second procedure for localization, is independent of clip position, and is a viable alternative to NLBB, especially in cases of extreme clip migration.

References

- [1] Burns RP. Image-guided breast biopsy. *Am J Surg* 1997;173:9-13.
- [2] Parker SH, Lovin JD, Jobe WE, et al. Stereotactic breast biopsy with a biopsy gun. *Radiology* 1990;176:741-7.
- [3] Velanovich V, Lewis FR, Nathanson SD, et al. Comparison of mammographically guided breast biopsy techniques. *Ann Surg* 1999;229:625-33.
- [4] Fuhrman GM, Cederbom GJ, Bolton JS, et al. Image-guided core-needle breast biopsy is an accurate technique to evaluate patients with nonpalpable imaging abnormalities. *Ann Surg* 1998;227:932-9.
- [5] Meyer JE, Smith DN, Lester SC, et al. Large-core needle biopsy of nonpalpable breast lesions. *JAMA* 1999;281:1638-41.
- [6] Israel PZ, Fine RE. Stereotactic needle biopsy for occult breast lesions: a minimally invasive alternative. *Am Surg* 1995;61:87-91.
- [7] Yim JH, Barton P, Weber B, et al. Mammographically detected breast cancer. Benefits of stereotactic core versus wire localization biopsy. *Ann Surg* 1996;223:688-700.
- [8] Burbank F. Stereotactic breast biopsy: comparison of 14- and 11-gauge Mammotome probe performance and complication rates. *Am Surg* 1997;63:988-95.
- [9] Burbank F, Forcier N. Tissue marking clip for stereotactic breast biopsy: initial placement accuracy, long-term stability, and usefulness as a guide for wire localization. *Radiology* 1997;205:407-15.
- [10] Smith LF, Henry-Tillman R, Rubio IT, et al. Intraoperative localization after stereotactic breast biopsy without a needle. *Am J Surg* 2001;182:584-9.
- [11] Krag D, Weaver D, Ashikaga T, et al. The sentinel node in breast cancer—a multicenter validation study. *N Engl J Med* 1998;339:941-6.

- [12] Lee CH, Egglin TK, Philpotts L, et al. Cost-effectiveness of stereotactic core needle biopsy: analysis by means of mammographic findings. *Radiology* 1997;202:849-54.
- [13] Liberman L, Fuhs MC, Dershaw DD, et al. Impact of stereotactic core breast biopsy on cost of diagnosis. *Radiology* 1995;195:633-7.
- [14] Bassett L, Winchester DP, Caplan RB, et al. Stereotactic core-needle biopsy of the breast: a report of the Joint Task Force of the American College of Radiology, American College of Surgeons, and College of American Pathologists. *CA Cancer J Clin* 1997;47:171-90.
- [15] Liberman L, Dershaw DD, Morris EA, et al. Clip placement after stereotactic vacuum-assisted breast biopsy. *Radiology* 1997;205:417-22.
- [16] Brenner RJ. Lesions entirely removed during stereotactic biopsy: preoperative localization on the basis of mammographic landmarks and feasibility of freehand technique—initial experience. *Radiology* 2000;214:585-90.
- [17] Reynolds HK. Marker clip placement following directional, vacuum-assisted breast biopsy. *Am Surg* 1999;65:59-60.
- [18] Rosen EL, Vo TT. Metallic clip deployment during stereotactic breast biopsy: retrospective analysis. *Radiology* 2001;218:510-6.
- [19] Homer MJ, Smith TJ, Safai H. Prebiopsy needle localization. Methods, problems, and expected results. *Radiol Clin North Am* 1992;30:139-53.
- [20] Fajardo LL, Bird RE, Hermann CR, Deangelis GA. Placement of endovascular embolization microcoils to localize the site of breast lesions removed at stereotactic core biopsy. *Radiology* 1998;206:275-8.
- [21] Burbank F. Stereotactic breast biopsy of atypical ductal hyperplasia and ductal carcinoma in situ lesions: improved accuracy with directional, vacuum-assisted biopsy. *Radiology* 1997;202:843-7.
- [22] Gray RJ, Salud C, Nguyen K, et al. Randomized prospective evaluation of a novel technique for biopsy or lumpectomy of nonpalpable breast lesions: radioactive seed versus wire localization. *Ann Surg Oncol* 2001;8:711-5.
- [23] Hastrich DJ, Dunn JM, Armstrong JS, et al. Diagnostic and therapeutic aspects of fine-wire localization biopsy for impalpable breast cancer. *Br J Surg* 1992;79:1038-41.
- [24] Rissanen TJ, Makarainen HP, Mattila SI, et al. Wire localized biopsy of breast lesions: a review of 425 cases found in screening or clinical mammography. *Clin Radiol* 1993;47:14-22.
- [25] Hasselgren PO, Hummel RP, Georgian-Smith D, Fieler M. Breast biopsy with needle localization: accuracy of specimen x-ray and management of missed lesions. *Surgery* 1993;114:836-42.
- [26] Mullen DJ, Eisen RN, Newman RD, et al. The use of carbon marking after stereotactic large-core-needle breast biopsy. *Radiology* 2001;218:255-60.
- [27] Marx M, Bernstein RM, Wack JP. Xylocaine plus methylene blue vs methylene blue alone for marking breast tissue preoperatively. *AJR Am J Roentgenol* 1993;160:896.